

1       **Claims**

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3       1.      Use of

4                 (a) a specific binding member which binds to a  
5                 cell death receptor or a nucleic acid encoding  
6                 said binding member and

7                 (b) a chemotherapeutic agent, wherein the  
8                 chemotherapeutic agent is a topoisomerase  
9                 inhibitor or a thymidylate synthase inhibitor  
10                in the preparation of a medicament for the  
11                treatment of a cancer, wherein the cancer is a  
12                cancer associated with a p53 mutation.

13

14       2.      The use according to claim 1 wherein the cancer  
15               is one or more of colorectal, breast, ovarian,  
16               cervical, gastric, lung, liver, skin and  
17               myeloid (e.g. bone marrow) cancer.

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19       3.      The use according to claim 1 or claim 2 wherein  
20               the death receptor is FAS.

21

22       4.      The use according to claim 1 or claim 2 wherein  
23               the binding member is an antibody or a fragment  
24               thereof.

25

26       5.      The use according to any one of the preceding  
27               claims wherein the binding member is the anti-  
28               FAS antibody CH11.

29

30       6.      The use according to any one of the preceding  
31               claims wherein said chemotherapeutic agent is  
32               an antifolate thymidylate synthase inhibitor or

- 1           a topoisomerase-I inhibitor.
- 2
- 3     7. The use according to any one of the preceding  
4       claims, wherein said chemotherapeutic agent is  
5       TDX or irinotecan (CPT-11).
- 6
- 7     8. The use according to any one of the preceding  
8       claims, wherein said specific binding member  
9       and chemotherapeutic agent are provided in  
10      concentrations sufficient to produce an RI of  
11      greater than 1.5.
- 12
- 13    9. A method of killing cancer cells having a p53  
14      mutation, said method comprising the separate,  
15      sequential or simultaneous administration to  
16      said cells of a therapeutically effective  
17      amount of a) a specific binding member which  
18      binds to a cell death receptor or a nucleic  
19      acid encoding said binding member and (b) a  
20      chemotherapeutic agent, wherein said  
21      chemotherapeutic agent is a topoisomerase  
22      inhibitor or a thymidylate synthase inhibitor.
- 23
- 24    10. A method of treating cancer cells having a p53  
25      mutation comprising the separate, sequential or  
26      simultaneous administration to a mammal in need  
27      thereof of a therapeutically effective amount  
28      of a) a specific binding member which binds to  
29      a cell death receptor or a nucleic acid  
30      encoding said binding member and (b) a  
31      chemotherapeutic agent, wherein said  
32      chemotherapeutic agent is a topoisomerase

- 1           inhibitor or a thymidylate synthase inhibitor.
- 2
- 3
- 4     11. The method according to claim 9 or claim 10  
5       wherein the cancer is one or more of  
6       colorectal, breast , ovarian, cervical,  
7       gastric, lung, liver, skin and myeloid (e.g.  
8       bone marrow) cancer.
- 9
- 10    12. The method according to claim 9, 10 or 11  
11      wherein the binding member is an antibody or a  
12      fragment thereof.
- 13
- 14    13. The method according to any one of claims 9 to  
15      12 wherein the death receptor is FAS.
- 16
- 17    14. The method according to any one of claims 9 to  
18      13 wherein the binding member is the anti-FAS  
19      antibody CH11.
- 20
- 21    15. The method according to any one of claims 9 to  
22      14 wherein said chemotherapeutic agent is an  
23      antifolate thymidylate synthase inhibitor or a  
24      topoisomerase-I inhibitor.
- 25
- 26    16. The method according to any one of claims 9 to  
27      15 wherein, wherein said chemotherapeutic agent  
28      is TDX or irinotecan (CPT-11) .
- 29
- 30    17. The method according to claim 16 wherein said  
31      specific binding member and chemotherapeutic  
32      agent are provided in concentrations sufficient

- 1           to produce an RI of greater than 1.5.
- 2
- 3       18. A product comprising a) a specific binding  
4           member which binds to a cell death receptor or  
5           a nucleic acid encoding said binding member and  
6           (b) a chemotherapeutic agent as a combined  
7           preparation for the simultaneous, separate or  
8           sequential use in the treatment of cancer,  
9           wherein said chemotherapeutic agent is a  
10          topoisomerase inhibitor or a thymidylate  
11          synthase inhibitor, and wherein the cancer  
12          cells comprise a p53 mutation.
- 13
- 14       19. A pharmaceutical composition characterised by  
15           the presence of a p53 mutation, wherein the  
16           composition comprises a) a specific binding  
17           member which binds to a cell death receptor or  
18           a nucleic acid encoding said binding member and  
19           (b) a chemotherapeutic agent, wherein said  
20           chemotherapeutic agent is a topoisomerase  
21           inhibitor or a thymidylate synthase inhibitor  
22           and (c) a pharmaceutically acceptable  
23           excipient, diluent or carrier..
- 24
- 25       20. The product according to claim 18 or the  
26           pharmaceutical composition according to claim  
27           19 wherein the cancer is one or more of  
28           colorectal, breast , ovarian, cervical,  
29           gastric, lung, liver, skin and myeloid (e.g.  
30           bone marrow) cancer.
- 31

- 1        21. The product according to claim 18 or claim 20  
2                  or the pharmaceutical composition according to  
3                  claim 19 or claim 20 wherein the binding member  
4                  is an antibody or a fragment thereof.
- 5
- 6        22. The product according to claim 18 or claim 20  
7                  or 21 or the pharmaceutical composition  
8                  according to claim 19 or claim 20 or 21 wherein  
9                  the death receptor is FAS.
- 10
- 11      23. The product according to claim 18 or any one of  
12                 claims 20 to 22 or the pharmaceutical  
13                 composition according to claim 19 or or any one  
14                 of claims 20 to 22 wherein the binding member  
15                 is the anti-FAS antibody CH11.
- 16
- 17      24. The product according to claim 18 or any one of  
18                 claims 20 to 23 or the pharmaceutical  
19                 composition according to claim 19 or or any one  
20                 of claims 20 to 23 wherein said  
21                 chemotherapeutic agent is an antifolate  
22                 thymidylate synthase inhibitor or a  
23                 topoisomerase-I inhibitor.
- 24
- 25      25. The product according to claim 18 or any one of  
26                 claims 20 to 24 or the pharmaceutical  
27                 composition according to claim 19 or or any one  
28                 of claims 20 to 24, wherein said  
29                 chemotherapeutic agent is TDX or irinotecan  
30                 (CPT-11) .
- 31

- 1       26. The product or pharmaceutical composition  
2       according to claim 25 wherein said specific  
3       binding member and chemotherapeutic agent are  
4       provided in concentrations sufficient to  
5       produce an RI of greater than 1.5.  
6  
7       27. A kit for the treatment of a cancer  
8       characterised by the presence of a p53  
9       mutation, said kit comprising a) a specific  
10      binding member which binds to a cell death  
11      receptor or a nucleic acid encoding said  
12      binding member and (b) a chemotherapeutic  
13      agent, wherein said chemotherapeutic agent is a  
14      topoisomerase inhibitor or a thymidylate  
15      synthase inhibitor and (c) instructions for the  
16      administration of (a) and (b) separately,  
17      sequentially or simultaneously.  
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19  
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